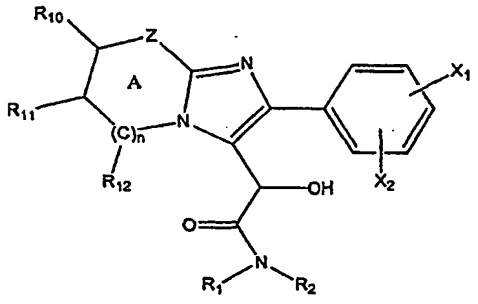
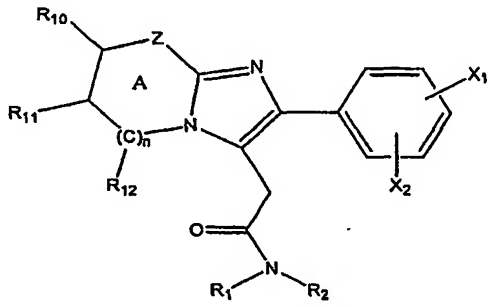
CLAIMS

What is claimed is:

1. A process for the preparation of a heteroaryl acetamide from a heteroaryl α-hydroxyacetamide, the process comprising directly hydrogenating the heteroaryl α-hydroxyacetamide in the presence of a strong acid, a halide and a catalyst, the heteroaryl α-hydroxyacetamide having the structure of Formula 1 and the heteroaryl acetamide having the structure of Formula 1A:



Formula 1



Formula 1A

wherein

Z is O, NR_{20} or CR_{21};

X_1 and X_2 are independently selected from the group consisting of hydrogen, halogen, C_{1-4} alkoxy, C_{1-6} alkyl, $-CF_3$ and CH_3SO_2-;

R_1 and R_2 are independently hydrogen or hydrocarbyl;

R_{10} is hydrogen, halogen, C_{1-4} alkyl, or a member of a fused ring wherein the fused ring is (i) a substituted or unsubstituted, saturated or unsaturated, five or six-membered, heterocyclic or carbocyclic ring fused to the A ring comprising R_{10}, the carbon atom to which R_{10} is attached, R_{20}, and the nitrogen atom to which R_{20} is attached, or (ii) a six-membered, aromatic, carbocyclic ring fused to the A ring comprising R_{10}, R_{11}, and the carbon atoms to which R_{10} and R_{11} are attached, optionally substituted with Y at a substitutable position thereof;

R_{11} is hydrogen, halogen, C_{1-4} alkyl, or a member of a fused ring wherein the fused ring is (i) a six-membered, aromatic, carbocyclic ring fused to the A ring comprising R_{10}, R_{11}, and the carbon atoms to which R_{10} and R_{11} are attached, optionally substituted with Y at a substitutable position thereof, or (ii) a

six-membered, aromatic, carbocyclic ring fused to the A ring comprising R_{11}, R_{12}, and the carbon atoms to which R_{11} and R_{12} are attached, optionally substituted with Y at a substitutable position thereof;

R_{12}, if present, is hydrogen, halogen, C_{1-4} alkyl, or a member of a fused ring wherein the fused ring is (i) a six-membered, aromatic, carbocyclic ring fused to the A ring comprising R_{11}, R_{12}, and the carbon atoms to which R_{11} and R_{12} are attached, optionally substituted with Y at a substitutable position thereof;

R_{20} is C_{1-5} alkyl or a member of a fused ring wherein the fused ring is a substituted or unsubstituted, saturated or unsaturated, five or six-membered, heterocyclic or carbocyclic ring fused to the A ring comprising R_{10}, the carbon atom to which R_{10} is attached, R_{20}, and the nitrogen atom to which R_{20} is attached;

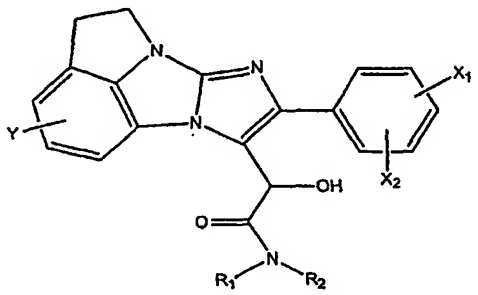
R_{21} is hydrogen, halogen or C_{1-4} alkyl;

n is 0 or 1;

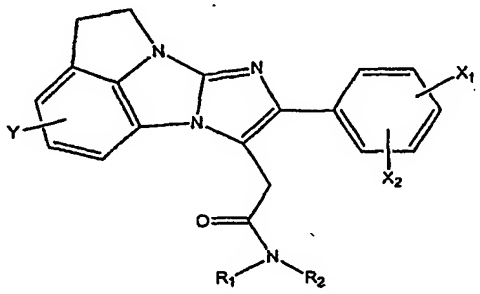
each Y is independently hydrogen, halogen or C_{1-4} alkyl; and

when Z is CR_{21}, the A ring is aromatic.

2. The process of claim 1 wherein the heteroaryl α-hydroxyacetamide has the structure of Formula 2 and the heteroaryl acetamide has the structure of Formula 2A



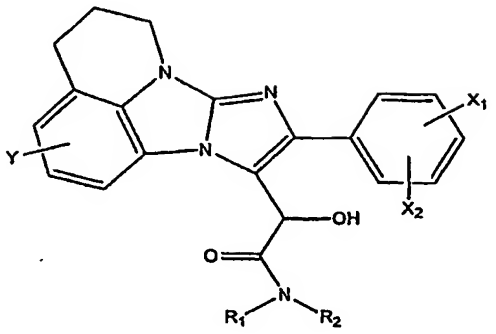
Formula 2



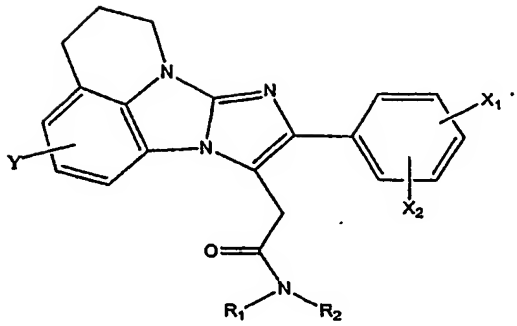
Formula 2A

wherein X_1 and X_2 are independently hydrogen or halogen, R_1 and R_2 are independently hydrogen or C_{1-5} alkyl, and Y is hydrogen, halogen or C_{1-4} alkyl.

3. The process of claim 1 wherein the heteroaryl α-hydroxyacetamide has the structure of Formula 3 and the heteroaryl acetamide has the structure of Formula 3A



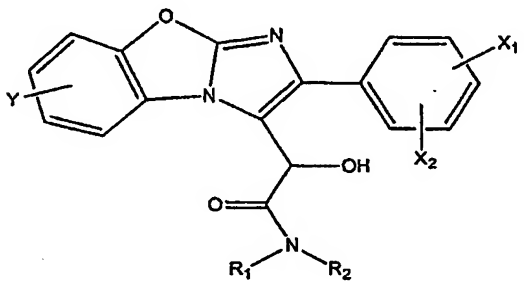
Formula 3



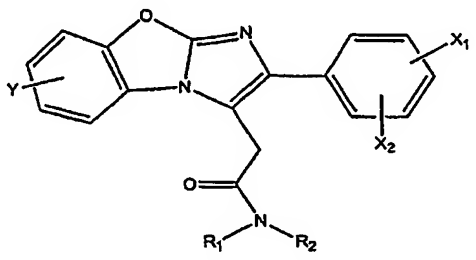
Formula 3A

wherein X_1 and X_2 are independently hydrogen or halogen, R_1 and R_2 are independently hydrogen or C_{1-5} alkyl and Y is hydrogen, halogen or C_{1-4} alkyl.

4. The process of claim 1 wherein the heteroaryl α-hydroxyacetamide has the structure of Formula 4 and the heteroaryl acetamide has the structure of Formula 4A



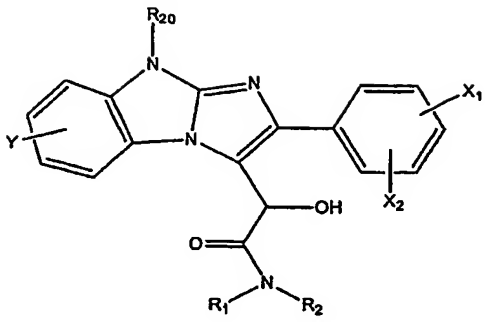
Formula 4



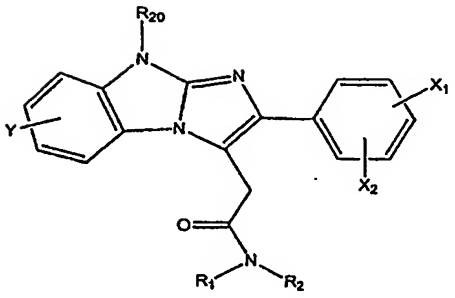
Formula 4A

wherein X_1 and X_2 are independently hydrogen or halogen, R_1 and R_2 are independently hydrogen or C_{1-5} alkyl and Y is hydrogen, halogen or C_{1-4} alkyl.

5. The process of claim 1 wherein the heteroaryl α-hydroxyacetamide has the structure of Formula 5 and the heteroaryl acetamide has the structure of Formula 5A



Formula 5

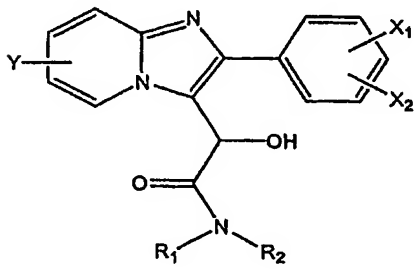


Formula 5A

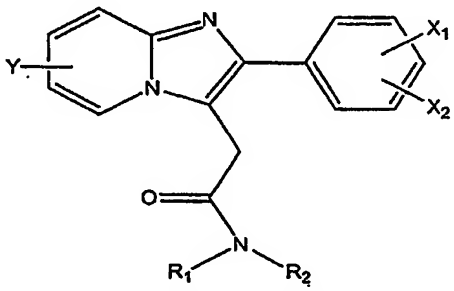
wherein X_1 and X_2 are independently hydrogen or halogen, R_1 and R_2 are independently hydrogen or C_{1-5} alkyl, R_{20} is C_{1-5} alkyl and Y is hydrogen, halogen or C_{1-4} alkyl.

6. The process of claim 1 wherein X_1 and X_2 are independently selected from the group consisting of hydrogen, halogen, C_{1-4} alkoxy and C_{1-6} alkyl, R_1 and R_2 are independently hydrogen or C_{1-5} alkyl and Y is hydrogen, halogen or C_{1-4} alkyl.

7. A process for the preparation of an imidazopyridine acetamide from an imidazopyridine α-hydroxyacetamide, the process comprising directly hydrogenating the imidazopyridine α-hydroxyacetamide in the presence of a strong acid, a halide and a catalyst, wherein the starting imidazopyridine α-hydroxyacetamide has the structure of Formula 6 and the product imidazopyridine acetamide has the structure of Formula 6A



Formula 6



Formula 6A

wherein

Y is hydrogen, halogen or C_{1-4} alkyl;

X_1 and X_2 are independently selected from the group consisting of hydrogen, halogen, C_{1-4} alkoxy, C_{1-6} alkyl, CF_3 and CH_3SO_2; and

R_1 and R_2 are independently hydrogen or C_{1-5} alkyl.

8. The process of claim 7 wherein Y is chloro or C_{1-4} alkyl.

9. The process of claim 7 wherein X_1 and X_2 are independently selected from the group consisting of hydrogen, halogen, C_{1-4} alkoxy and C_{1-6} alkyl.

10. The process of claim 7 wherein Y is C_{1-4} alkyl, X_1 and X_2 are independently hydrogen or C_{1-6} alkyl and R_1 and R_2 are C_{1-5} alkyl.

11. The process of claim 10 wherein Y is methyl, X_1 and X_2 are independently hydrogen or methyl and R_1 and R_2 are methyl.

12. The process of claim 7 wherein the strong acid has a pK_a relative to water of about -9 or less.

13. The process of claim 12 wherein the strong acid is perchloric acid or sulfuric acid.

14. The process of claim 13 wherein the strong acid is sulfuric acid.

15. The process of claim 7 wherein the halide is a chloride or bromide ion.

16. The process of claim 15 wherein the imidazopyridine α-hydroxyacetamide, the strong acid, the halide, and the catalyst form a mixture that has a chloride or bromide concentration of about 2.1×10^{-5} M to 1.8×10^{-4} M or less.

17. The process of claim 15 wherein the halide is a bromide ion.

18. The process of claim 7 wherein the halide is provided by a halide source that is any halide salt that does not interfere with the purification of the product.

19. The process of claim 18 wherein the halide source is an alkali metal halide, alkaline earth metal halide, transition metal halide or a halide salt of an organic cation.

20. The process of claim 19 wherein the halide source is an alkali metal bromide, alkali metal chloride, alkaline earth metal bromide, alkaline earth metal chloride, transition metal bromide, transition metal chloride or bromide or chloride salts of an organic cation.

21. The process of claim 18 wherein the halide source is a bromide salt where the cation does not interfere with the purification of the product.

22. The process of claim 21 wherein the halide source is LiBr, NaBr, KBr, $MgBr_2$, $CaBr_2$ or NH_4Br.

23. The process of claim 22 wherein the halide source is LiBr or KBr.

24. The process of claim 7 wherein the catalyst is a solid catalyst.

25. The process of claim 24 wherein the catalyst is a precious metal catalyst.

26. The process of claim 25 wherein the catalyst is a platinum group metal catalyst.

27. The process of claim 26 wherein the catalyst is a palladium catalyst.

28. The process of claim 27 wherein the catalyst is palladium on barium sulfate, palladium on carbon, palladium on alumina, palladium on strontium carbonate, palladium on barium carbonate or palladium on calcium carbonate.

29. The process of claim 28 wherein the catalyst is palladium on barium sulfate or palladium on carbon.

30. The process of claim 29 wherein the catalyst is palladium on barium sulfate.

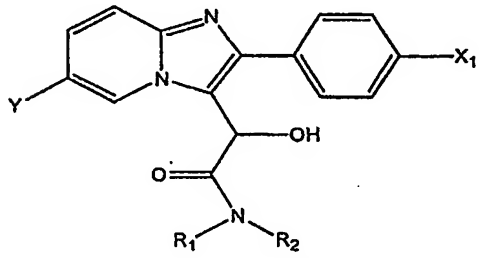
31. The process of claim 7 wherein the starting heteroaryl α-hydroxyacetamide, the catalyst, the strong acid and the halide are dissolved in a solvent that is a carboxylic acid or alcoholic solvent.

32. The process of claim 31 wherein the solvent is methanol, ethanol, n-propanol, formic acid, acetic acid, ethanoic acid or propionic acid.

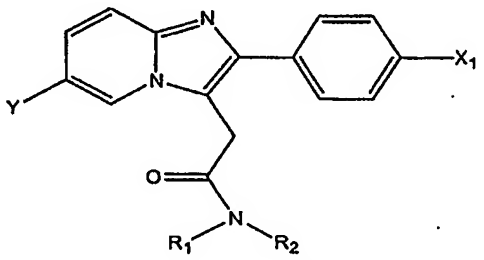
33. The process of claim 31 wherein the solvent is a carboxylic acid.

34. The process of claim 33 wherein the solvent is acetic acid.

35. A process for the preparation of an imidazopyridine acetamide from an imidazopyridine α-hydroxyacetamide, the process comprising directly hydrogenating an imidazopyridine α-hydroxyacetamide in the presence of hydrogen gas, a strong acid or mixture of strong acids with a pKa of about -9 or less, a chloride or bromide ion and a palladium catalyst, wherein the imidazopyridine α-hydroxyacetamide has the structure of Formula 7 and the imidazopyridine acetamide product has the structure of Formula 7A.



Formula 7



Formula 7A

wherein

Y is C_{1-4} alkyl;

X_1 is C_{1-4} alkyl; and

R_1 and R_2 are independently hydrogen or C_{1-5} alkyl.

36. The process of claim 35 wherein Y, X_1, R_1 and R_2 are methyl.

37. The process of claim 35 wherein the bromide or chloride ion is a bromide ion.

38. The process of claim 37 wherein the bromide ion is provided by a bromide source of LiBr, NaBr, KBr, $MgBr_2$, $CaBr_2$ or NH_4Br.

39. The process of claim 38 wherein the bromide source is KBr.

40. The process of claim 35 wherein the palladium catalyst is palladium on carbon or palladium on barium sulfate.

41. The process of claim 40 wherein the palladium catalyst is palladium on barium sulfate.

42. The process of claim 35 wherein the imidazopyridine α-hydroxyacetamide, the strong acid, the chloride or bromide ion and the palladium catalyst is dissolved in a solvent of methanol, ethanol, n-propanol, formic acid, acetic acid, ethanoic acid or propionic acid.

43. The process of claim 42 wherein the solvent is formic acid, acetic acid, ethanoic acid or propionic acid.

44. The process of claim 43 wherein the solvent is acetic acid.

45. The process of claim 35 wherein the process is carried out at a reaction temperature of about 40°C to about 100°C.

46. The process of claim 45 wherein the reaction temperature is about 50°C to about 80°C.

47. The process of claim 45 wherein the reaction temperature is about 70°C to about 75°C.

48. The process of claim 35 wherein the process is carried out at a reaction pressure of about 1 atmosphere to about 4 atmospheres.

49. The process of claim 48 wherein the reaction pressure is about 1 atmosphere to about 3 atmospheres.

50. The process of claim 49 wherein the reaction pressure is about 2.0 atmospheres to about 2.8 atmospheres.

51. The process of claim 36 wherein the strong acid is sulfuric acid, the bromide or chloride ion is bromide and the catalyst is palladium on barium sulfate.